

INCORPORATION OF GENETIC MARKERS INTO THE METRIC  
PHYSICAL MAP OF HUMAN CHROMOSOME 19

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The physical map of human chromosome 19 is comprised of ordered sets of contigs spanning ~90% of the chromosome. Over 70% of the chromosome is covered with cosmid contigs mapped by EcoR1 restriction enzyme digestion. A metric FISH order map incorporating over 200 reference cosmids (average spacing of <240kb) from these contigs has been constructed. Thus, the order of, and gap size between, contigs is known. Genes and ESTs are assigned to cosmids/contigs in the map as they are identified. The utility of this physical map is further enhanced by the assignment of genetic markers to cosmids included in the metric physical map. Over 150 polymorphic markers have been assigned to cytogenetically mapped cosmids. This includes ~100 PCRable markers with heterozygosities of >0.50 and also >90% of the markers included in available linkage maps. Inclusion in the metric physical map can resolve the order of tightly linked genetic markers or markers from different linkage maps, and provides estimates of physical distances among markers. The published linkage map is ~120cM (sex-equal), or twice the physical size of the chromosome; interesting discrepancies in the estimated physical and genetic distances are noted. For example, the genetic distance between some pairs of markers in the p13.3 and q13.4 regions is 10-15 times the estimated physical distance. Significant clustering of markers is also noted; for example, eight highly informative markers map within a region of less than 800kb in p13.1. The cosmids from the metric physical map provide unique resources for generating additional genetic markers that are precisely mapped within defined regions. The integration of the genetic and physical maps allows for refined localization and focused screening for potential candidate genes when searching for disease genes. Work performed under auspices of the US DOE by the Lawrence Livermore National Laboratory; contract No. W-7405-ENG-48

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